ACIDITY OF STOMACH SECRETIONS IN HUMANS, RATS, AND PIGS, and THE POTENTIAL IMPORTANCE OF STOMACH pH IN BIOAVAILABILITY OF Pb IN SOILS AND MINE WASTES.

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Questions have been raised about which experimental animal species might be appropriate models for the risk to infants/children of the Pb in urban soils, mine wastes, Pb-ore concentrates, smelter wastes, and Pb-paint contaminated soils. Because of the potential effect of stomach acidity on rate of dissolution of some forms of environmental Pb, a review of stomach pH was undertaken. This text can be considered an extension of the review by Chaney, Mielke, and Sterrett (1989) on speciation and bioavailability of soil Pb. I was asked to evaluate stomach pH of humans, pigs, and rats, because of the apparent importance of stomach pH in dissolution of PbS and soil Pb, and the indications from some scientists interested in these questions that rats may differ so much from humans in stomach pH that research conducted with rats would not provide information useful to risk analysis for human ingestion of soil and mine wastes. Many Superfund sites involve mine wastes which appear to contain predominantly PbS; if PbS has low bioavailability to humans under normal environmental exposure conditions for the worst case children, the cost of remediating smaller areas at these Superfund sites may be much less than if the Pb in the mine waste/soil is considered to be as bioavailable as that in soils contaminated by smelter emissions, automotive emissions, or paint residues. These latter sources have been found to cause increased PbB in children exposed to soils when soil Pb exceeds 500-1000 mg/kg (CDC, 1985; EPA, 1989 OSWER directive; EPA, 1986 Air Quality Criteria Documents; Duggan and Inskip, 1985). Pb-B in children exposed to PbS in mine wastes or ore concentrates appeared to have substantially lower response to this source than seen in other populations exposed to more soluble Pb species in soil or dust (Middaugh et al., 1989; Steele et al., 1990).

Research has repeatedly shown that PbS dissolution is very dependent upon pH. The chemical solubility of PbS responds to both pH and particle size (Healy et al., 1982; Roy, 1977). Because of the short incubation of diet in the stomach, and possibly because of the pH buffering of food, mine wastes, and PbS, larger particle size materials should not be expected to be dissolved in the stomach. In the early 1900's tests were conducted to evaluate dissolution of PbS vs other Pb compounds in gastric juice of a human volunteer. PbS was very much less soluble than Pb carbonates and sulfates under the test conditions (Carlson and Woefel, 1913; Woefel and Carlson, 1914). Short term feeding tests by Barltrop and Meek (1975; 1979) using rats showed a strong difference between Pb compounds and that larger particles of paint or PbS had lower bioavailability. However, in one feeding trial with humans, small amounts of finely divided PbS were fed to fasting volunteers (Rabinowitz et al, 1980). The subjects absorbed the Pb isotope from this test material as well as they absorbed Pb nitrate from fasting stomach. Unfortunately, Rabinowitz et al. did not test the absorption of PbS mixed with food. Food would be expected to buffer stomach pH enough to sharply reduce dissolution of PbS. Perhaps a higher dose, more similar to that which might be ingested by *pica* children would have raised stomach pH, or a larger particle size more similar to environmental PbS, may have reduced the apparent bioavailability of ingested PbS by fasting adults. Chamberlain et al. (1978) appear to have fed fine PbS with food and found about 6-12% absorption; I have

not seen this British report.

Several approaches were used to search for information about species difference in stomach pH. I began by looking up references in the microelement nutrition literature which have considered the pH of the stomach and the duodenum in order to develop *in vitro* Fe bioavailability assays. microelement nutrition specialists were contacted (Miller et al., 1981; Schricker et al, 1981; Reddy et al., 1988). I was referred to scientists at the National Children's Nutrition Research Center (USDA-ARS, Houston, TX) for more specific data about children. I checked with swine nutritionists for more data on pigs, and with other animal nutritionists for data on rats.

During this reading, I found that perhaps the most difficult part of dealing with stomach pH is the need to consider both the fasting condition and the effect of food (or soil) on pH of the stomach contents. The number generally described as the pH of the stomach is the pH of gastric fluid secreted by fasting individuals. Actually, much is known about this because the importance of gastric fluid pH on ulcer development in humans. Hereditary, hormonal and dietary influences on gastric acid secretion cause pH to vary from 1.0 to 2.5 (or even as high as 7 with poor ability to secrete stomach acid, e.g. achlorhydria; Bezwoda et al., 1978). However, as soon as food is ingested, the buffering capacity of the food causes the pH of the stomach contents to rise (Longstreth et al., 1975; Malagelada et al., 1976; Malagelada et al, 1977; Malagelada et al., 1979). Many of the techniques were developed and studies were conducted to learn more about the nature of ulcer disease in humans, a result of excessive gastric acid secretion or sensitivity of stomach or duodenal tissues to stomach acid. Compounds used to counteract ulcer inhibit acid secretion, and raise the pH of the stomach (e.g. Lucey et al., 1989). Antacids also react with gastric acids to raise stomach pH. Surely soil would also cause the pH of the stomach to rise. Presence of $CaCO_3$, especially finely divided $CaCO_3$ in calcareous soils, but also neutral soils with higher cation exchange capacity, would cause a similar rise in pH of the stomach contents.

In searching for further information about stomach pH of pigs, etc., I contacted swine nutritionist Dr. Normal Steele, USDA-ARS. He noted that pigs may maintain a higher pH in the stomach because of the amount of saliva secreted.

I contacted Dr. Walter Mertz, Chairman of the Human Nutrition Research Center at Beltsville to find names of some experts on stomach pH of children. He referred me to Dr. Peter Reeds of the Children's Nutrition Research Center, Houston. He in turn referred me to Dr. Rob Shoreman. Shoreman suggested that the normal gastric pH is 1-2 in each rats, pigs, and children. Textbooks on pediatric gastrointestinal physiology include 2 edited by E. Levinthal. He referred me to Dr. Susan Henning, a specialist in gastrointestinal physiology and development who had been doing some work Pb absorption from milk by infant rats as part of her research on development of gastrointestinal functions.

In discussion with Dr. Susan Henning (713-798-7084), Childrens' Nutrition Research Center at Bailor University, I learned about her work on uptake of Pb from milk by infant rats. Infant (pre-weaning, < 24 days old) rats have high stomach pH (6-7), and the transition to strongly acidic stomach pH is delayed compared to children (Takeuchi et al, 1981;). She found that ^{203}Pb added to rat milk is mostly bound by casein, and that passage through the infant rat stomach does not separate Pb from the casein. She also found that most of the enhanced Pb uptake rate of the infant rat (80% compared to <10 % in adult rats fed the same milk test diets) occurs in the ileum (probably by pinocytosis), rather than in the duodenum where Pb uptake occurs in older animals. She felt

that, in general, everything about gastrointestinal physiology in the pig is closer to humans than is that of the rat. This is especially so in the infant rat before weaning where stomach acidity is extremely different from pigs and humans. However, she did not believe data were available to show that 100-150 g rats were an appreciably less appropriate dietary model for 18 month old children than weaned pigs would be. (She referred me to two rat stomach experts, Dr. L. Litchenberger at Univ. Texas [713-792-5279] and Dr. Leonard R. Johnson at Memphis [901-528-7088]).

I was able to contact Dr. L.R. Johnson who had done extensive research on gastrointestinal physiology with rats. He noted that a likely source of possible misunderstanding about stomach pH results from the way we manage rats. The fasting rat stomach fluid pH is 1-1.5; however, the rat usually eats intermittently/continuously (nibbles), and much data about rat stomach pH shows a higher pH level because food is present in the stomach. The human eats meals, and accumulates a "basal" gastric fluid of pH 1-2 in the antrum of the stomach. But when food is ingested, the pH rises to 5-6. The rat continuously secretes stomach acid, and secretion responds to several hormone activities. The human has a low basal secretion, but hormones significantly increase acid secretion when food in ingested or the stomach is distended. When fed rat chow, rat stomach empties slower than do human stomachs, but this may be an artifact of the highly digestible type human foods compared to rat chow. He feels that rat and human stomach pH levels are not that dissimilar, and that rats are a valid model for processes which are pH dependent such as PbS dissolution. Both secrete a solution which is about 150 mM HCl. He referred me to a general old paper of his on acid secretion by the rat (Proc. Soc. Exp. Biol. Med. 131:186-188, 1969), but thought this has no specific data about stomach pH, but may cite some. He felt we would be wise to test the pH of stomach contents of rats, people, and pigs fed the purified diet generally agreed necessary for valid assessment of soil Pb bioavailability.

I contacted Dr. Phyllis Johnson, USDA-ARS-Grand Forks Human Nutrition Lab, a nutritionist who collaborates with me on bioavailability of food Cd. After noting the aspects of PbS, soil Pb, stomach pH, effect of food, etc., we discussed appropriateness of animal models for soil Pb bioavailability to humans. She knew of no specific reason to reject the rat in favor of the pig since both have basal gastric fluid pH similar to humans, and likely have similar pH of gastric fluid + purified diet (AIN-76 Purified diet has low buffer capacity compared to many foods). One point came from this discussion that might be of importance to with meal/between meal soil-Pb risk. It is possible that the acid secretion pattern of rats, pigs, or humans given meals may be somewhat different than the same animals given food *ad lib*. In testing the with meal, between meal comparison, one might need to consider 3 groups: 1) soil-Pb vs. Pb-acetate supplied mixed with food, supplied *ad lib*; 2) soil-Pb vs. Pb-acetate supplied mixed with food to meal-fed animals; and 3) soil-Pb vs. Pb-acetate supplied after fasting (between meals) to meal-fed animals.

In discussion with Dr. George W. Bates (Texas A&M University), I learned about stomach pH of pigs ingesting a pinto bean meal. Dr. Bates has been studying the bioavailability of food Fe, and trying to develop *in vitro* methods to assess the bioavailability of Fe. Their *in vivo* work used cannulated 'Sinclair' miniature pigs he could feed test meals and sample gastric fluid and duodenal fluid. He has not measured the pH of the stomach fluids before or long after food introduction in his experiments. A pinto bean meal caused stomach pH to be 5.1, 4.0, and 3.1 at 30, 60, and 90 minutes after introduction of the homogenized slurry of pinto beans test meal (not by

stomach tube) (Reddy et al., 1988). These pH levels are very similar to the results for adult humans from Malagelada et al. (1976; 1979). In earlier work on *in vitro* Fe bioavailability, Bates used pH 2 to simulate stomach (Kojima et al., 1981; ; upon finding the pH of pinto bean digesta did not go below 3, he has now switched to pH 3 for the *in vitro* work as well (Reddy et al., 1988).

There have been a few studies of the absorption of Pb by swine. Most of the work involved very high feed Pb concentrations to examine Pb toxicity. Practical diets were used rather than purified diets which allow much higher Pb bioavailability. Link and Pensinger (1966) described Pb toxicity in swine. Hsu et al. (1975) examined the factorial interaction of dietary Ca (0.7% vs. 1.1%) with toxic levels of Pb (1000 mg/kg) and Zn (4000 mg/kg) in swine. Higher dietary Ca reduced blood and bone Pb and Zn; however, increased dietary Zn increased Pb deposition and toxicity. The test diets were begun at 4 weeks (about 7.5 kg), and fed for 9 or 13 weeks. Sharma et al. (1982) evaluated Pb deposition in food tissues of several species of livestock, including swine. Because they used only about 5 and 25 mg Pb/kg addition to practical basal ration which contained 2 mg Pb/kg, they found little change in tissue Pb. The test diets were fed for 12 weeks. There was no change in Pb in skeletal muscles, but Pb level in bone, liver, and kidney were increased in relation to increasing dietary Pb dose. Younger pigs had somewhat higher levels of bone Pb than did finishing pigs fed the same diets. Upon cessation of the test diets, Pb in kidney and liver dropped to background levels. At the levels tested, Pb had no effect on gain or feed consumption.

CONCLUSION:

Stomach pH of rat, pig, and human children are not different enough to justify use of pig rather than rat in assessing bioavailability of Pb in soils and mine wastes. Considering that 6-10 replicate animals are required for each dose of each material to be tested, pigs would require more expensive facilities or longer time to obtain needed information on the effect of soil and mine waste properties on the bioavailability of Pb in these materials. Rats are appropriate for the more extensive studies, while important principles should be confirmed in pigs. Because of the potential extreme public expense in remediating Pb polluted urban soils and mine wastes, selected very important principles might need to be confirmed in primates to win public acceptance of these costs.

Under the conditions normally recommended for rat bioassays of Pb bioavailability (120 g animals, long after weaning; 30 day feeding; purified diet; sub-toxic maximum dose), rats, weaned pigs, and children with significant risk from soil Pb (> 12 months), have very similar stomach pH. Each secretes gastric acid with about 100-150 mM HCl (pH 1.3-1.5) in response to digestion hormones. However, perhaps also very important, food and soil can buffer the pH of the stomach to high levels, > pH 6, greatly reducing dissolution of environmental PbS. Limestone in soil or mine wastes, or higher cation exchange capacity neutral pH soils might consume gastric acidity and thus allow the digesta to enter the small intestine without receiving the strong acid attack normally assumed to take place in the stomach.

ANNOTATED BIBLIOGRAPHY

Agunod, M., N. Yamaguchi, R. Lopez, A.L. Luhby, and G.B.J. glass. 1969. Correlative study of hydrochloric acid, pepsin, and intrinsic factor secretion in newborns and infants. Am. J. Dig. Dis. 14:400-414.

Examined secretion of acid, pepsin, and intrinsic factor in human infants aged 0.5-90 days old. The infants were given gastric hormone stimulation and gastric output was evaluated by stomach tube. Newborn infants had poor secretion. However, by 2-3 months, the acid secretion was within the range of normal for adults, although the mean was lower than the mean for normal adults.

Alino, S.F., D. Garcia, and K. Uvnas-Moberg. 1986. Effect of intragastric pH, prostaglandins and prostaglandin synthesis inhibitors on the release of gastrin and somatostatin into the gastric lumen of anaesthetized rats. Acta Physiol. Scand. 126:1-8.

During perfusion of the rat stomach with dextran solution at pH 6, vagal stimulation at 10 Hz decreased perfusate pH to 1.3, and gastrin and somatostatin were released at a ratio of 2:1.

Allcroft, R. 1950. Lead as a nutritional hazard to farm livestock. IV. Distribution of lead in the tissues of bovines after ingestion of various lead compounds. J. Comp. Path. 60:190-208.

Fed different Pb compounds at different rates to calves and adult cattle. Included finely ground galena, red lead, basic Pb carbonate, wet paint, shot, fine metal dust, and acetate. Pb-B was increased much less by PbS than by other Pb compounds (except Pb shot) in short term studies. In longer term feeding studies, PbS was absorbed less than Pb shot. Stomach pH in cattle is much higher than non-ruminant rats, pigs, and humans, and Pb absorption is substantially less in ruminants.

Barltrop, D. and Meek, F. 1975. Absorption of different lead compounds. Postgrad. Med. J. 51:805-809.

Barltrop, D. and Meek, F. 1979. Effect of particle size on lead absorption from the gut. Arch. Environ. Health 34:280-285.

Fed several particle sizes of PbS to rats in an acute (500 mg Pb/kg diet) bioassay of bioavailability. Based of Pb-B measurements after 48 hr exposure, they found that absorption was increased 5-fold in 6 μm diameter PbS compared to 196 μm PbS.

Bezwoda, W., R. Charlton, T. Bothwell, J. Torrance, and F. Mayet. 1978. The importance of gastric hydrochloric acid in the absorption of nonheme food iron. J. Lab. Clin. Med. 92:108-116. /Copy/Summ.

Collected gastric fluid from fasting individuals. pH ranged from 1 to near 7, with nearly all in the range of 1 to 2.3. Examined the ability of gastric fluid and HCl to dissolve labelled Fe from a white bread sample. Both HCl and gastric fluid fit a singe curve with smooth increase in soluble Fe as pH went below 2. White bread, however, has little pH buffering capacity.

Carlson, A.J. and A. Woefel. 1913. The solubility of white lead in human gastric juice, and its bearing on the hygiene of the lead industries. Am. J. Public Health 3:755-769.

Obtained paint dust from Pb carbonate and Pb sulfate paints, from paint dust as well as pigment sources used in paints. They obtained gastric juice from a human via gastric fistula; the total acidity varied from 0.40 to 0.52%. They tested the solubility of Pb from Pb-carbonate and Pb-sulfate pigments and paints in the gastric juice, and then did some feeding studies with dogs and cats. The Pb-carbonate materials were much more soluble and appreciably more toxic than the Pb-sulfate materials. They concluded that 1) the state should aim at elimination of the use of Pb-carbonate in all industries, and 2) workers should be supplied a glass of milk between meals.

Chamberlain, A.C., M.J. Heard, P. Little, D. Newton, A.C. Wells, and R.D. Wiffen. 1978. Investigations Into Lead From Motor Vehicles. A.E.R.E. Report R-9188. H.M.S.O., London.

Chaney, R.L., H.W. Mielke, and S.B. Sterrett. 1989. Speciation, mobility, and bioavailability of Soil Lead. [Proc. Intern. Conf. Lead in Soils: Issues

and Guidelines. B.E. Davies & B.G. Wixson (eds.)]. Environ. Geochem. Health 11(Supplement):105-129.

Chidambaram, M.V., M.B. Reddy, J.L. Thompson, and G.W. Bates. 1989. In vitro studies of iron bioavailability: Probing the concentration and oxidation-reduction reactivity of pinto bean iron with ferrous chromogens. Biol. Trace Element Res. 19:25-40.

Deren, J.S. 1971. Development of structure and function in the fetal and newborn stomach. Am. J. Clin. Nutr. 24:144-159.

Review on development of stomach physiology in different species with focus on humans. In humans, gastric acid secretion begins in the fetus. In the rat, acid secretion begins at about day 25, just after weaning. In the pig, acid secretion begins in the fetus. He reviewed available papers on acid secretion in human infants, and calculated the secretion per kg body weight. Although very young infants have weak acid secretion, by age 2-3 months the acid secretion/kg has reached about half of the adult level. By 12-18 months the secretion is not different from adults, and this is the critical age range for most sensitive children (peak Pb-B in Cincinnati longitudinal study).

Duggan, M.J., & Inskip, M.J. 1985. Childhood exposure to lead in surface dust and soil: A community health problem. Public Health Rev. 13:1-54.

A detailed review of the potential of soil and dust Pb to cause risk to children. Independent calculation of the slope of the Pb-Blood:Pb-Soil ratio for many studies in the literature.

Ghai, O.P., M. Singh, B.N.S. Walia, and N.G. Gadekar. 1965. An assessment of gastric acid secretory response with "maximal" augmented histamine stimulation in children with peptic ulcer. Arch. Dis. Child. 40:77-?.

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Healy, M.A., P.G. Harrison, M. Aslam, S.S. Davis, and C.G. Wilson. 1982. Lead sulphide and traditional preparations: Routes for ingestion, and solubility and reactions in gastric fluid. J. Clin. Hosp. Pharm. 7:169-173.

PbS is used as a false medicine and as a cosmetic by some persons in the Moslem world. Use of PbS as an eye cosmetic ("surma") by children has lead to elevated Pb-B. They believe the main route of exposure is through hand contact and transfer to the mouth. They conducted a study of the dissolution of different PbS preparations in water, saliva, and simulated gastric fluid (composition not shown). They measured dissolution of two samples of PbS cosmetic, 30 ± 20 μm and 100 ± 20 μm average diameter, in actual human gastric fluid (properties not reported). The finer material was dissolved much more quickly than was the coarser material. Both materials were much finer than the normal size of lead mine wastes which contain PbS.

Henning, S.J. 1981. Postnatal development: Coordination of feeding, digestion, and metabolism. Am. J. Physiol. 241:G199-G214.

Review on rat development. Provided references to literature on timing of development of acid secretion in rats vs. other species.

Hsu, F.S., L. Krook, W.G. Pond, and J.R. Duncan. 1975. Interactions of dietary calcium with toxic levels of lead and zinc in pigs. J. Nutr. 105:112-118.

Kojima, N., D. Wallace, and G.W. Bates. 1981. The effect of chemical agents, beverages, and spinach on the in vitro solubilization of iron from cooked pinto beans. Am. J. Clin. Nutr. 34:1392-1401.

Kovacs, T.O.G., J.H. Walsh, V. Maxwell, H.C. Wong, T. Azuma, and E. Katt. 1989. Gastrin is a major mediator of the gastric phase of acid secretion in dogs: Proof by monoclonal antibody neutralization. Gastroenterol. 97:1406-1413.

Using monoclonal antibody to gastric, showed that secretion of acid (mmol/15 min), normally increased by IV gastrin, was prevented when the monoclonal antibody was injected IV.

Link, F.S. and R.R. Pensinger. 1966. Lead toxicosis in swine. Am. J. Vet. Res. 27:759-763.

Longstreth, G.F., J.-R. Malagelada, and V.L.W. Go. 1975. The gastric response to a transpyloric duodenal tube. Gut 16:777-780. /Copy/Summ.

Tested method to sample the fluids in stomach and duodenum. Determined acid secretion, gastric emptying time, etc., with duodenal tube in the stomach or in the duodenum. Found no significant change due to placing duodenal sampling tube. Test meal, homogenized, was pH 6.0; comprised of 80 g steak, 0.1 g salt, 25 g white bread, 60 g vanilla ice cream with 35 h chocolate syrup = 400 mL.

Lucey, M.R., J.A.H. Wass, L.H. Rees, A.M. Dawson, and P.D. Fairclough. 1989. Relationship between gastric acid and elevated plasma somatostatinlike immunoreactivity after a mixed meal. Gastroenterol. 97:867-872. /Copy/Summ.

Measured the effect of IV cimetidine on stomach pH and blood hormones and immunoproteins associated with excessive stomach acidity and ulcer. Stomach fluid pH was 2.0 with an intragastric infusion of isotonic saline, and rose to 3.7 with provision of cimetidine. Addition of 0.1 N HCl to the isotonic saline, with IV cimetidine, cause stomach fluid pH to be about 3.3.

Malagelada, J.-R., V.L.W. Go, and W.H.J. Summerskill. 1979. Different gastric, pancreatic, and biliary responses to solid-liquid or homogenized meals. Dig. Dis. Sci. 24:101-110. /Copy/Summ.

Using individuals fitted with gastric and duodenal sampling tubes, they measured pH, acid secretion, food transit, and other phenomena in persons supplied a "normal" meal vs. those fed a homogenized meal. Normal meals elicited a stronger early gastric secretion response, and resulted in higher gastric acidity and volume than homogenized meals. Gastric fluid pH before the meal averaged about 2.0; the pH rapidly rose to near 5, and slowly fell over a 2 hr period to about 1.8. Titriable acidity of the stomach contents rose as pH fell. During the bulk of the stomach digestion period of about 1 hr, the pH exceeded 4.0.

Malagelada, J.-R., G.F. Longstreth, W.H.J. Summerskill, and V.L.W. Go. 1976. Measurement of gastric functions during digestion of ordinary solid meals in man. Gastroenterol. 70:203-210. /Copy/Summ.

Report on development of the methods used in their subsequent research. Sample fluid in the stomach and the duodenum every 10 minutes. Show effect of ingesting normal food on pH of the gastric contents. A meal causes gastric pH to rise to 4-5 within 15 min.; pH declines slowly and does not reach basal pH 2.0 until over 1.5 hr.

Malagelada, J.-R., G.F. Longstreth, T.B. Deering, W.H.J. Summerskill, and V.L.W. Go. 1977. Gastric secretion and emptying after ordinary meals in duodenal ulcer. Gastroenterol. 73:989-994. /Copy/Summ.

Compared normal people with gastric ulcer patients, using the method they developed to sample gastric and duodenum fluids every 10 min. Ulcer patients had an "inappropriately prolonged gastric secretory response to meals". Further, gastric fluid was delivered to the duodenum sooner and in larger quantities in the ulcer patients. Food caused stomach fluid pH to rise to about 5, and pH declined to abut 1.5 after about 2 hr.; initial and final pH levels were lower for the ulcer patients, and pH declined sooner after feeding the test meal.

Middaugh, J.P., C. Li, and S.A. Jenkerson. 1989. Health hazard and risk assessment from exposure to heavy metals in ore in Skagway, Alaska. Final Report, Oct. 23, 1989. State of Alaska Dept. Health and Social Services. /

Miller, D.D., B.R. Schricker, R.R. Rasmussen, and D. Van Campen. 1981. An in vitro method for estimation of iron availability from meals. Am. J. Clin. Nutr. 34:2248-2256.

Miller, E.R. and D.E. Ulley. 1987. The pig as a model for human nutrition. Ann. Rev. Nutr. 7:361-382.

Thorough review of use of pig as animal model for human nutrition. Many aspects considered, and

references provided. For many reasons dealing with absorption of nutrients, pigs are judged to be one of the best models for nutritional physiology of humans. However, there was no consideration of heavy metals, nor of stomach pH.

Rabinowitz, M.B., J.D. Kopple, and G.W. Wetherill. 1980. Effect of food intake and fasting on gastrointestinal lead absorption in humans. Am. J. Clin. Nutr. 33:1784-1788.

Tested the retention of Pb stable isotopes by humans who ingested several chemical forms of Pb, including freshly formed PbS. Added NaS to solution of stable isotope; rinsed finely divided precipitate to remove excess NaS. Fed PbS, $Pb(NO_3)_2$, and Pb-cysteine complex (? how formed) to fasting persons, who retained 37 ± 6.1%, 30.8 ± 19.4%, and 30.0 % of dose, while about 10.3 ± 2.2% was retained when the Pb was fed with food. Doses were 144-221 µg Pb/day, equal to the background ingestion of Pb before the volunteers began the study. This indicates that finely divided PbS, fed to fasting humans, was as bioavailable as soluble Pb salts. However, other research indicates that gastric pH is strongly affected by presence and buffering ability of the food. Similarly, phytate and Ca+P from foods can precipitate dietary Pb.

Reddy, M.B., E.J. Browder, and G.W. Bates. 1988. Cannulated swine and in vitro approaches to iron bioavailability. pp 173-185. In A.S. Prasad (ed.). Essential and Toxic Trace Elements in Human Health and Disease. A.R. Liss, Inc., New York. /Copy/

Present research on digestion of Fe from pinto bean test meal by miniature swine used as model for human digestion of dietary Fe. The pH of the gastric contents rose to 5.1 by 30 min. after the bean slurry was supplied to the pigs, and fell slowly. Food can raise stomach pH substantially in pigs.

Reddy, M.B., M.V. Chidambaram, J. Fonseca, and G.W. Bates. 1986. Potential role of in vitro iron bioavailability studies in combatting iron deficiency: A study of the effects of phosvitin on iron mobilization from pinto beans. Clin. Physiol. Biochem. 4:78-86.

Rodbro, P., P. Krasilnikoff, P.M. Christiansen, and V. Bitsch. 1966. Gastric secretion in early childhood. Lancet 2:730-731.

Studied normal healthy children aged 11-30 months of age. Used newer method to assess acid secretion in which digestive hormones are injected so that the ability of the test subjects to secrete acid is evaluated, the method already in use for study of adults. This work evaluated older children than described in the Agunod et al. 1969 study of newborn children. A naso gastric tube was used to sample the stomach contents after administration of hormone. The children secreted significantly less acid than normally secreted by adults. Other workers (Doran, 1971; Figure 1) calculated acid secretion per kg body weight, and found that the amount of acid secreted meq/hr/kg by children was quite similar to adults.

Rodbro, P., P.A. Krasilnikof, and P.M. Christiansen. 1967. Parietal cell secretory function in early childhood. Scand. J. Gastroenterol. 2:209-?.

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Roy, B.R. 1977. Effects of particle sizes and solubilities of lead sulphide dust on mill workers. Am. Ind. Hyg. Assoc. J. 38:327-332.

15 mill workers were sampled for exposure using personal air samplers, and Pb-B. There was little relationship between apparent exposure to total or respirable dust and Pb-B. The galena examined had an accessory rock of dolomitic limestone. Samples of ore concentrate, screened to 200 mesh, were dissolved under varied conditions of pH, time, and temperature. Used pH 1.3 or 1.8 HCl to simulate gastric juice. In some, neutralized this solution after incubation overnight. Only 0.77-1.89 (mean 0.84) % of ore Pb was dissolved under the conditions studied. If neutralized, most then precipitated. pH 1.3 is 0.1 N HCl, commonly believed to be the pH of human fasting gastric juice. Exact details of the extractions are not clear from the text (15 g ore conc., + unknown volume of acid, with either HCl of known strength added or the mixture adjusted to known pH).

Schricker, B.R., D.D. Miller, R.R. Rasmussen, and D. Van Campen. 1981. A comparison of in vivo and in vitro methods for determining availability of iron from meals. Am. J. Clin. Nutr. 34:2257-2263.

Sharma, R.P., J.C. Street, and J.L. Shupe. 1982. Translocation of lead and

cadmium from feed into edible tissues of swine. J. Food Safety 4:151-163.

Spenney, J.G. 1979. Physical chemical and technical limitations to intragastric titration. Gastroenterol. 76:1025-1034.

Detailed review of the methods to measure gastric acid secretion. Depending on the endpoint pH used in the titration, significant error can be introduced. Discussion of normal acidity of stomach in relation to making these measurements.

Steele, M.J., B.D. Beck, B.L. Murphy, and H.S. Strauss. 1990. Assessing the contribution from lead in mining wastes to blood lead. Regulat. Toxicol. Pharmacol. In press.

Detailed review of the nature of Pb in mine wastes, and the available data which indicate that PbS has lower solubility and bioavailability than "soil Pb" or "dust Pb".

Takeuchi, K., W. Peitsch, and L.R. Johnson. 1981. Mucosal gastrin receptor. V. Development in newborn rats. Am. J. Physiol. 240:G163-G169.

Study of development of acid secretion and sensitivity to gastrin in rats in relation to development. Rats normally have poor acid secretion until about the time of weaning. At that time, acid secretion begins to approach adult levels, with stomach pH about 1.5-2. Injection of gastrin to pre-weaned rats did not induce the normal acid secretory response to this hormone. This work showed that the rat tissues are not sensitive to gastrin, and do not have surface receptors for this hormone, until about the time of weaning, about 20 days after birth.

Woefel, A., and A.J. Carlson. 1914. The solubility of lead sulphide ores and of lead sulphide in human gastric juice. J. Pharmacol. Exper. Ther. 5:549-552. /Copy/Summ.

Questions of magnitude of difference between PbS and White Pb (basic Pb carbonate) caused them to obtain data on PbS similar to their earlier data on carbonate and sulfate of Pb. They had a human with permanent gastric fistula. They gave him food to get him secreting stomach acid, and collected the gastric fluid for solubility testing. They obtained ore concentrates from Missouri, about 70% Pb. They combined 0.5 g Pb test material, 25 mL gastric juice, and 25 mL distilled water; incubated for 10 hr at 38°. The % of Pb dissolved from the Federal Concentrator = 2.84; from the Deloge Concentrator = 1.38; from the St. Joseph Pb Co. = 3.32; (ores averaged 2.5%); while laboratory grade PbS = 4.65. These were somewhat lower than Pb-sulfate = 5.7%, and Pb-carbonate = 48%. The authors emphasized that PbS was indeed soluble in gastric juice, and might be able to cause excessive PbB in workers, the original question being examined.

OTHER REFERENCES CONSIDERED.

Beach, J.R. and S.J. Henning. 1988. The distribution of lead in milk and the fate of milk lead in the gastrointestinal tract of suckling rats. Pediatr. Res. 23:58-62.

Henning, S.J. 1987. Functional development of the gastrointestinal tract. pp. 285-300. In L.R. Johnson (ed.) Physiology of the Gastrointestinal Tract. Second Edition. Raven Press, New York.

Henning, S.J. and L.C. Cooper. 1988. Intestinal accumulation of lead salts and milk lead by suckling rats. Proc. Soc. Exp. Biol. Med. 187:110-116.

Henning, S.J. and L.L. Leeper. 1984. Duodenal uptake of lead by suckling and weanling rats. Biol. Neonate 46:27-35.

Henning, S.J. and L.L. Leeper. 1984. Effect of cortisone on intestinal uptake of lead in the suckling rat. Biol. Neonate 46:249-253.

Schulman, R.J., S.J. Henning, and B.L. Nichols. 1988. The miniature pig as an animal model for the study of intestinal enzyme development. Pediatr. Res. 23:311-315.

Papers sent to me by Dr. C.P. Weis (EPA, Region 8) to support selection of pig as test animal for Pb bioavailability testing with soil and mine wastes:

Miller, E.R. and D.E. Ulley. 1987. The pig as a model for human nutrition. Ann. Rev. Nutr. 7:361-382.

Newport, M.J. and M.J. Henschel. 1984. Evaluation of the neonatal pig as a model for infant nutrition: Effects of different proportions of casein and whey protein in milk on nitrogen metabolism and composition of digesta in the stomach. Pediatr. Res. 18:658-662.

Reports digestion of liquid milks with different concentration of protein and different ratios of casein and whey proteins. Test diets were fed for 18 days from birth; 1 hr after a feed, the pigs were killed and stomach contents obtained for examination. Among mostly nitrogen balance information, they report the pH of stomach contents. From their Table 6:

Feed Intake mL/kg/day	Casein:Whey ratio of diet 80:20		40:60		
	15	30	15	30	Protein (g/L)
	---Stomach pH 1 hr after feed---				
250	3.01	3.48	2.81	2.90	
375	2.82	2.92	2.83	2.71	

Houpt, K.A., T.R. Houpt, and W.G. Pond. 1979. The pig as a model for the study of obesity and of control of food intake: A review. Yale J. Biol. Med. 52:307-329.

Review of regulation of food intake by pig as model for human. No information about stomach pH.

Fleming, S.E. and D. Arce. 19 . Using the pig to study digestion and fermentation in the gut. Reference not provided on reprint.

Evaluation of food movement through the pig using cannula in the digestive system and in the portal vein and caretid artery. Observed transfer of nutrients into the blood in relation to digestion. Measured volatile fatty acid absorption, and volatile gas emissions. Used Yucatan miniature swine. Tested control fiber free diet vs three diets with 40% variously modified red kidney beans. No information about stomach pH in this paper.

Moazam, F., R.L. Miller, B.M. Rodgers, J.L. Talbert, and J.E. McGuigan. 1980. Fasting and postprandial serum gastrin in neonatal swine and changes following antrectomy. J. Surg. Res. 28:39-43.

Neonatal swine show little increase in secretion of the hormone "gastrin" in response to eating. Adults show marked secretion of gastrin in response to feeding, and gastrin induces increased volume of secretion of gastric acid into the stomach of most mammals. No measurements of gastric acid secretion were made in this research. No information about stomach pH of pigs in this paper. Other species have shown no response of stomach to injected gastrin in the neonate compared to adults or weanlings.

Cheng, S.-F., R.J. Schanler, and H.-P. Sheng. 1989. The miniature piglet as a model for the assessment of calcium bioavailability. Pediatr. Res. 25:286A. Abstract only.

Tested Ca absorption by neonatal miniature pigs as model for Ca absorption by preterm human infants. Concluded useful model regarding Ca supplements for milk to be fed to preterm infants. No information about pH of stomach.

Dodds, W.J. 1982. Symposium Report: The pig model for biomedical research. Fed. Proc. 41:247-256.

Discussion of nutrition, disease, physiology, etc. of pig compared to human. No information about stomach pH in any report at symposium.

Papers on role of gastric mucus and the mucus-bicarbonate barrier to protect the tissue which lines the stomach from stomach acid.

Williams, S.E. and L.A. Turnberg. 1980. Retardation of acid diffusion by pig gastric mucus: A potential role in mucosal protection. Gastroenterol. 79:299-304. [Microelement Bioavailability: Gastric Mucus Barrier - Misc. Auth. /Copy/Summ.

Conducted diffusion experiments to determine whether gastric mucus from pig stomach served as a diffusion barrier to acid. Found that mucus delayed diffusion. So did filter paper. Stops flow. Serves as an unstirred layer through which diffusion must occur.

Quigley, E.M.M. and L.A. Turnberg. 1987. pH of the microclimate lining human gastric and duodenal mucosa in vivo. Gastroenterol. 92:1876-1884.

Examined luminal and juxtamucosal pH in different positions along the digestive tract in humans ± duodenal ulcer. Always found pH near the mucosa was nearer neutral than was the lumen. Believed due to mucus-bicarbonate barrier. Ulcer patients were less able to maintain neutral zone adjacent to the mucosa than were normal persons. Gastric fundus: 2.01 ±0.17 in lumen but 4.84 ± 0.37 at mucosa; gastric body: 1.82 ± 0.12 in lumen but 5.5 ±0.15 at mucosa; gastric antrum: 3.52 ± 0.34 but 5.42 ±0.29 at mucosa. When the stomach was perfused with pH 2.0 saline, similar difference. If perfused with pH 1.5, some of the differences declined.

Ross, I.N. and L.A. Turnberg. 1983. Studies of the "mucus-bicarbonate" barrier on rat fundic mucosa: The effects of luminal pH and a stable prostaglandin analogue. Gut 24:1030-1033.

When fluid was 2.0, mucosal layer pH was as high as 7.0. Supports buffer secretion concept. Used excised, perfused stomach of rat.